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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/866,488	05/25/2001	Anthony E. Bolton	033136-179	4401

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EXAMINER	
YU, MISOOK	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/866,488	BOLTON ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2005 and 20 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-30 and 46-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-30 and 46-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 20 July, 2005 20 April 2005, 10 January 2005, and 20 January 2004 is acknowledged.

Claim 19 is amended, and claims 46-59 are new. Claims 19-30, and 46-59 are pending and under consideration.

This Office action contains new grounds of rejection.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

The rejection of claim 19-30 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendment.

The rejection of claims 19-30 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for method of treating CHS, does not reasonably provide enablement for any other diseases listed in claim 19 is withdrawn in view of the amendment.

The Following Are New Grounds of Rejection

Double Patenting

Claims 19-30, 58, 59 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 16-28 of Application 09/866,569 (recently allowed, but U.S. Patent No. has not been assigned as of 10/17/2005). Although the conflicting claims are not identical,

they are not patentably distinct from each other because the Application 09/866,569 at Paragraph 2 under Example 2 clearly communicates that alleviation of a patient's symptom of congestive heart failure of a patient suffering from congestive heart failure is due to reduced level of inflammation. Therefore, instant claim 9 is a generic claim for claim 16 of the allowed case. One-way obviousness applies to double patenting rejection. Further, the product being administered is identical in both cases. Therefore, both methods inherently result in treating inflammation and/or congestive heart failure.

Claim Rejections - 35 USC § 112

Claim 59 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 59 is confusing because the purpose set out in preamble of the claim, and conclusion step of the active steps do not match. For the purpose of this Office action, the Office treats that the active step trumps over the preamble. However, this treatment does not relieve applicant the burden of responding to this rejection.

Claims 58, and 59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the

time the application was filed, had possession of the claimed invention. This is a new matter rejection. The Office is unable to location the support for the limitation "congestive heart failure" in new claims 58, and 59. Applicant is kindly requested to point out the support in the specification as originally filed.

Claims 46-57 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for how to make and use the apoptotic bodies and/or apoptotic cells made from mice fibroblasts for treatment of mice contact hypersensitivity, one of T-cell-mediated and inflammatory disorders in a mammalian patients (Figure, and Example 1 and 2 of the specification), does not reasonably provide enablement for use of the instant invention in treatment and/or prophylaxis of inflammation in autoimmune disorders in mammalian patient.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 46-57 are drawn to the use of apoptotic bodies and/or apoptotic cells in treatment and/or prophylaxis for inflammation in autoimmune diseases.

Applicant argues that the new claims 46-57 are drawn to treatment of inflammation resulting from autoimmune diseases, not teating the underlying cuase itselt. This argument has been fully considered but found unpersusaive because the full scope of the instantly claimed method is prevention and treatment of inflammation from notoriously difficult human diseases and the

specification does not provide any in vivo model of any of the diseases except CHS. The art, for example Lui et al (1999, Human Immunology vol. 60, pages 568-74) recognizes a great deal of unpredictability in the cause the the symptoms asociated the autoimmune disease. See the first sentence of Liu et al. The specification is limited to how to make and use apoptotic cells for treating mice with CHS, which is not a model for multiple sclerosis, rheumatoid arthritis, or any other disease listed in the instant claims.

The factors which must be considered in determining undue experimentations are set forth in In re Wands USPOQ2d 1400. The factors include 1) quantity of experimentation necessary, 2) the amount of guidance presented, 3) the presence or absence of working example, 4) the nature of the invention, 5) the state of the prior art, 6) the predictability of the art, 7) breath of the claims.

Teaching of the instant specification is limited to mice contact hypersensitivity. Although inducing apoptosis in mammalian cells are known in the art as listed at page 7, last two lines to page 8 of the specification, the specification fails to teach what is appropriate choice and treatment of cells to make the appropriate apoptotic cells and/or apoptotic bodies for reducing inflammation in each diseases listed in claim 46. Based on at page 9 lines 14-19, i.e. "appropriate levels of treatment of the cells to create apoptotic bodies for use in the present invention depend to some extent on the nature of the chosen cells and cellular composition, and the type of treatment chosen to induce apoptosis" and "the specific dose employed will, of course, be dependent upon

the age, weight and severity of the disease in the treated patient all of which are within the skill of the attending clinician" from page 11, last line to page 12, lines 1 and 2, one of skill in the art would have to resort to undue experimentation in order to practice the full scope of the claimed invention. There is no evidence that the range specified in claims 55-57 are useful range of treating and/or preventing inflammation in any diseases listed in the claim 46 except CHS. In summary, with regard to factors 1) and 2) above undue experimentation is required to determine how to make and use the claimed invention (claims 46-57) for reducing inflammation in each of the disease listed in claim 46.

The claims as currently construed say that "apoptotic cells" are panacea for prevention of inflammation for psoriasis, rhematoid arthritis, lupus, and other diseases whose underlying causes are not well understood in the current state of art. For example, Sardjnon et al., Arthritis Rheum. 2005 Oct;52(10):3220-9, which is published 5 years after the effective filing date of the instant application, discloses one mice model system. Comparing the teaching of Sardjnon et al., and what is being disclosed in the instant specification, one of skill in the art would not accept the efficacy of the claimed method even reducing inflammation, let alone preventing inflammation in multiple sclerosis, rheumatoid arthritis, and others.

It is noted that use of apoptotic cells and/or apoptotic bodies is not accepted treatment for reducing inflammation for rheumatoid arthritis, psoriasis, or diabetes mellitus. Therefore, the determination of the specific dosage is within the skill of one in the art. It might take years through lengthy clinical trials for

research clinicians to determine (1) which source of the cells to make apoptotic cells and/or apoptotic bodies for each of specific diseases, (2) a specific dose for any one of the diseases listed in claim 46. Treating and preventing inflammation associated with autoimmune disease are research state, i.e. one of skill in the art is trying to figure out what causes the inflammation associated with autoimmune disease, and developing mice model for research and development of an agent to treat inflammation associated with autoimmune disease Note Sardjono et al (cited above). Therefore those skilled in the art would have reason to doubt unsupported assertions of successful treatment methods for inflammation of those diseases. With regard to factors 4), 5), and 6) above, there is a great deal of unpredictability in the treatment and/or prophylaxis of inflammation in those diseases in claim 46 because the precise mechanism of the diseases listed in claim 46 is not well understood (Lui et al), and Sardjono et al). It is noted that law requires that the disclosure of an application shall inform those skilled in the art how to use applicants' alleged discovery, not how to find out how to use it for themselves. With factors 3) and 7) above it is noted that no working example is present to indicate that claimed invention could be used in treatment and prevention of inflammation of any of the disease listed in the claim 46 except CHS.

Considering the state of art for prevention and treating the diseases, it is maintained that one skilled in the art would have reasons to question the efficacy of the claimed treatment/prevention method in the absence of working examples or other evidence of the claimed method's effectiveness. Applicant is invited to

present scientific data showing that the full scope of the claims is enabled. Limiting the scope of the claims to method of treating CHS with the recited active step would also obviate the rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MISOOK YU, Ph.D.
Examiner
Art Unit 1642